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Towards the Construction of a Resistance Risk Evaluation Scheme*

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Abstract: Pesticide resistance management needs an indication of the risk of resistance developing in pests against pesticide applications. This paper describes an evaluation system for the ranking of these risks. The term pests includes all organisms which are causing economic damage in agriculture, including weeds and plant pathogens. The system distinguishes six broad risk categories. It is based on expert judgement of answers to a maximum of ten questions on crop husbandry, pest biology and pest control. The system has been developed for registration purposes in The Netherlands, and is currently being discussed within the European and Mediterranean Plant Protection Organisation (EPPO).

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1 INTRODUCTION

Resistance against pesticides is an ever-increasing phenomenon in agriculture. It is defined as failure to control pests under field conditions with formerly effective doses of a pesticide. Pests are defined here as any living organisms, which are to be controlled, including diseases and weeds. There is an increase in the incidence of resistance and in the number of pesticides which are no longer useful.[1–3] Thus resistance management is increasingly necessary.[4,5] In order to develop and carry out resistant management strategies, which must always relate to strategies of pesticide use, one has to have indications of the risks of resistance development.

This paper describes a resistance risk evaluation system which is meant to provide quick insight into the resistance risks of specific pesticide applications on specific pests. It cannot be used to gain insight into the inherent resistance risks at the chemistry level, as is often determined by means of in-vitro laboratory tests. The system is based on qualitative expert judgement. It ranks risks in five broad categories: neglible, low, moderate, high and very high. Additionally, there is the category of risk unknown. By answering, at most, ten questions, a resistance risk category is arrived at.

The project leading to the development of this evaluation scheme was initiated by the Dutch Ministry of Agriculture to provide a base for resistance risk evaluations as a part of the registration process of pesticides as demanded in EU Directives 91/414/EC and 93/71/EC. The system is currently under discussion for use in Europe.

2 RISK CATEGORIES

2.1. *Risk very low* applies to all active ingredients which have been used extensively for at least 30 years in situations where resistance should have appeared

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but has not, or has appeared only sporadically, and/or resistant biotypes are highly unfit.

2.2. *Risk low* is indicated where both the inherent characteristics of the active ingredient(s), and especially the cropping system and pest involved, give only remote chances of resistance arising.

2.3. *Risk moderate* applies where factors operate which facilitate resistance development, but are countered by other factors.

2.4. *Risk high* applies to those situations where it is likely that resistance will appear comparatively quickly if no active resistance management takes place.

2.5. *Risk very high* applies to those situations in which both the inherent characteristics of the chemical and the agronomic system select strongly for resistance in a pest which easily adapts genetically.

2.6. *Risk unknown* is reserved for those cases where both the occurrence of resistance and the mode of action are unknown, as is often the case with novel compounds.

3 QUESTIONS

Figure 1 shows the general layout of the procedure used to assess resistance risk. The basic questions to be answered are stated below. Some questions appear in more than one place in Fig. 1 because they are on a pathway to a different risk category, arising from differing answers to earlier questions.

1. *Does the formulated product contain a single, or more than one, active ingredient?*

Discrimination of these two options is important, because mixtures may exert a much lower selection pressure than single products.

2. *Has resistance against the active ingredient been reported over the last 30 years?*

Some compounds have been in use for many years without evidence of any serious resistance problems evolving and the risk should then be considered very low.

3. *Does the mixture comply with the criteria posed for mixtures?*

Mixtures are made for very different purposes, of which resistance management is but one. The criteria relating to the latter are that the active ingredients should:

a. control the same pest spectrum with comparable effectiveness;
b. have the same biological persistance relating to pest phenology;
c. have different target sites;
d. be degraded in a different manner and
e. preferably exert negative cross-resistance and/or synergism.

Mixtures not meeting these criteria are treated as single products for which the most resistance-prone partner is evaluated further and this determines the risk status of the mixture.

4. *Is the crop in which the product is applied grown continuously?*

In answering this question the most relevant consideration is the continuity of a development niche for the pest concerned. Crops considered to be grown continuously in the context of this evaluation are:

a. all perennial crops;
b. all crops grown year-round in protected environments;
c. all crops grown in very close (biological) vicinity to the same, or very similar, host crops;
d. all annual field crops grown without rotations, or grown in very limited (ineffective) rotations;
e. weed control on industrial sites, railway tracks, roads etc.

5 and 15. Is the pest a major pest?

Discrimination between major and minor pests in this context is based on a consideration of the pest's ecology, with all biotic and abiotic factors involved, and taking into consideration whether or not the pest concerned will practically always cause economic damage to the crop if control measures are not taken.

6 and 16. Is the pest controlled by chemical means only?

In this question the crop protection system should be considered with a view that systems relying solely on chemical control are more prone to resistance than systems which rely to a degree on non-chemical control.

7 and 17. Do all available active ingredients used to control the organism to be evaluated belong to the same, or different resistance groups?

Again, unilateral dependence on one system, in this case one resistance group, is considered more risky than reliance on several groups. In many cases, mode of action is identical to mode of resistance, but not always, because resistance based on metabolic detoxification by the target organism should be included where possible.

8, 11 and 18. Is resistance known against the active ingredient or any other registered active ingredient used in a similar situation and belonging to the same resistance group?

With the answer to this question, worldwide knowledge on resistance status of the pesticide (group) is accounted for in the evaluation. In-vitro resistance is considered to be far less important than the proven existence of field resistance, because in-vitro resistance has, in the past, often not been a very reliable indicator of the development of resistance in the field.

9, 10, 12, 13, 19 and 20. What is the biological persistence of the evaluated compound? How frequently will the compound be applied under worst-case conditions? How specific is the mode of action?

Question			*Proceed to*
1	a.	product contains one active ingredient	2
	b.	product contains more than one active ingredient	3
2	a.	the active ingredient has been in use for more than 30 years without any evidence of resistance	**risk negligible**
	b.	resistance known, or not known but active ingredient in use for less than 30 years	4
3	a.	mixture satisfies mixing criteria	**risk negligible**
	b.	mixture does not satisfy mixing criteria	2
4	a.	crop grown continuously	5
	b.	crop grown in rotation	15
5	a.	major pest	6
	b.	minor pest	**risk low**
6	a.	integrated control	14
	b.	chemical control only	7
7	a.	all active ingredients currently in use to control the pest in the crop concerned belong to one resistance group	8
	b.	registered active ingredients belong to more than one resistance group	11
8	a.	resistance known in the field, from laboratory data or from active ingredients belonging to the same resistance group	9
	b.	resistance not known, mode of action known	10
	c.	novel compound, resistance and mode of action unknown	**risk unknown**
9	a.	persistent active ingredient with specific mode of action, or active ingredient applied frequently	**risk very high**
	b.	non-persistent active ingredient with specific mode of action or active ingredient not applied frequently	**risk high**
	c.	active ingredient with a non-specific mode of action	**risk moderate**
10	a.	persistent active ingredient with specific mode of action or active ingredient applied frequently	**risk high**
	b.	non-persistent active ingredient with specific mode of action or active ingredient not applied frequently	**risk high**
	c.	active ingredient with a non-specific mode of action	**risk low**
11	a.	resistance known in the field, from laboratory data to active ingredients belonging to the same resistance group	12
	b.	resistance not known, mode of action known	13
	c.	novel compound; resistance and mode of action unknown	**risk unknown**
12	a.	persistent active ingredient with specific mode of action or active ingredient applied frequently	**risk high**
	b.	non-persistent active ingredient with specific mode of action or active ingredient not applied frequently	**risk moderate**
	c.	active ingredient with a non-specific mode of action	**risk moderate**
13	a.	persistent active ingredient with specific mode of action or active ingredient applied frequently	**risk high**
	b.	non-persistent active ingredient with specific mode of action or active ingredient not applied frequently	**risk moderate**
	c.	active ingredient with a non-specific mode of action	**risk low**
14	a.	active ingredient is an important control factor in the integrated control system; persistent in nature, and has a specific single mode of action	**risk moderate**
	b.	other compounds	**risk low**
15	a.	minor pest in one crop only, no volunteer plants in succeeding crops	**risk negligible**
	b.	minor pest in all crops	**risk low**
	c.	major pest in one crop only	16
	d.	major pest in all crops of the rotation concerned	6
16	a.	chemical control only	17
	b.	integrated control	**risk low**
17	a.	all registered active ingredients currently in use to control the pest in the crop concerned belong to one resistance group	18
	b.	registered active ingredients belong to more than one resistance group	**risk low**
18	a.	resistance known in the field, from laboratory data or to active ingredients belonging to the same resistance group	19
	b.	resistance not known, mode of action known	20
	c.	novel compound, resistance and mode of action unknown	**risk unknown**
19	a.	persistent active ingredient with specific mode of action or active ingredient applied frequently	**risk high**
	b.	non-persistent active ingredient with specific mode of action or active ingredient not applied frequently	**risk moderate**
	c.	active ingredient with non-specific mode of action	**risk low**
20	a.	persistent active ingredient with specific mode of action or active ingredient applied frequently	**risk moderate**
	b.	other active ingredients	**risk low**

Fig. 1. General procedure for assessing resistance risk.

In these questions we consider biological persistence and frequency of application as having similar selection effects; especially because it is not the chemical persistence asked for, but the biological persistence. Compounds exerting selection pressure during a long period (in population dynamic terms) are considered to be risky. The same holds true for certain highly specific modes of action which are prone to monogenic resistance.

14. Is the claimed product an important factor in integrated pest management (IPM)?

IPM has become almost a magical term which is often misused. In this question one has to estimate the proportion of mortality of the pest caused by the evaluated molecule as compared to the mortality caused by the other control methods used. If the compound under evaluation causes a disproportionately high part of the mortality, the system is considered to be non-IPM.

4 DISCUSSION

The appearance of resistance in field populations is dependent on two separate events; first the incidence of resistance genes (whether present through mutation or existing incidence is not important here) and second selection pressure.[1,2] The incidence of resistance genes cannot be influenced and is dependent on the pesticide itself and the organism concerned.

However, the selection pressure on resistance genes present in a pest population in the field is under human control. It is the farmer who grows his crop in a specific crop husbandry system on which the pests are dependent for the development of their populations, and who controls these pest populations using cultural, non-chemical and chemical methods. All these actions exert selection pressures on the pest. If selection pressure is very much centred on one aspect, such as pesticide resistance, it is a function of genes present, population size, pest biology and time which will determine the moment the whole population will shift genetically towards resistance.[1,2,6]

Because resistance development is mainly a matter of selection pressure, any risk evaluation system is forced towards evaluating selection pressure in the crop husbandry systems where it is exerted. In examining selection pressure in agriculture, we noticed that there is a certain hierarchy of factors. On top of the system is the farming system, which determines the available niches for pests. Pest niche importance is also determined to a high degree by pest biology, so farming system and pest biology together indicate the need for control measures. Control is composed of many different possible measures and an insight is needed as to how far the pest population considered is kept under control, by which means and to what degree. Ideally, a complete population dynamic quantification of the farming system, pest biology and control measures would give an accurate indication of the selection pressure involved. Combined with quantified incidence rates and/or mutation rates of resistance genes in the field, this would allow calculation of specific resistance risks. Development of such a system would be a huge task and would have to be done for every pesticide application registered. Field circumstances vary greatly, which would lead to a broad scatter of resistance risks. It is very likely that cost considerations alone would make the exercise impossible. Moreover, we need risk indications to distinguish those situations of pesticide applications which merit our intense attention, because of their high risk for resistance development, from other situations in which risk is low and needs little attention.

We think therefore that a fully quantified system is hardly possible, and moreover is not needed for the purpose of distinguishing low-risk situations from high-risk situations.

In developing our evaluation system we soon realised how different resistance management approaches can sometimes be between the disciplines of, e.g. plant pathology, entomology and weed science. Even more interesting was the discovery that resistance risk evaluation can be done with the same questions for all disciplines, but we very well realise that the required interpretations based on expert judgement are different for the different disciplines. In other words, there remains a need for clarification and explanation of the different questions for use by the different disciplines. We are preparing papers for the different disciplines in which we will give practical examples of the uses of the scheme.

Some criteria could simply be derived from others, as was the case with the question about mixing: criteria for herbicide mixtures used in resistance management have been formulated by Wrubel and Gressel in 1994,[7] and we extrapolated them to all other pesticides since we have not observed any fundamental difference in their application.[1,2,4]

In other fields, much knowledge is simply lacking, and working on the scheme made us even more aware of the many existing gaps in knowledge. For instance, knowledge on resistance grouping based on similar degradation pathways is still in its infancy. In order to develop, explain and use resistance management systems, we need the ability to distinguish between high- and low-risk resistance situations. We think that the evaluation scheme presented provides useful guidance for expert use in the ranking of resistance risks.

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